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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,501	06/15/2006	Vamsi Krishna Mootha	WIBL-P01-013	3194

28120 7590 09/21/2010

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PATENT DOCKETING 39/41
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
09/21/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Applicant filed a response to the Final Action of March 2, 2010 on August 30, 2010.

Claims filed August 30, 2010 have not amendments. Claims 2-16, 18-41, 43-46, 48-77, 79-92, 94-105 are cancelled. Claims 1, 17, 42, 47, 78, 113, 114 are withdrawn.

Claims 93, 106-112, 115-127, drawn to a method for identifying an agent that regulates expression of OX-PHOS genes, are under consideration.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 93, 106-112, 115-121, 124-127 remain rejected under 35 U.S.C. 102(b) as being anticipated by Attie et al., WO 02/22886, published March 21, 2002, for reasons of record, March 2, 2010.

For Applicant's convenience, the rejection of March 2, 2010 has been copied below.

Attie et al. teach that that a microarray was used to determine gene expression patterns in adipose tissue of obese individuals and diabetic individuals, by using the mouse model (Attie et al., page 3, parag. 00012). Attie et al. teach that Tables 1, 2, and 3 summarize the results of this analysis. Table 1 lists the genes for which decreased levels of gene expression was found with increasing obesity in each mouse strain. Table 2 shows the list of genes that increase in expression with increased obesity. Table 3 lists the changes in gene expression that correlated with the development of hyperglycemia. Table 1

shows that there are groups of genes, including those associated with mitochondrial function (Attie et al., page 4, parags 00015-00016, Table 1, pages 12-13). "Similar to succinate dehydrogenase" (mouse accession number aa245912, human accession number NM_003000) is the same as SDHB and "similar to cytochrome c1" (mouse accession number aa466050, human accession number BC001006) is the same as CYC1 (see NCBI printouts, Homo sapiens cytochrome c-1, mRNA, NCBI [online], 2006 [retrieved on 2010-02-25]. Retrieved from the Internet:< URL: http://www.ncbi.nlm.nih.gov/nuccore/12654366>, pages 1-4, and Homo sapiens succinate dehydrogenase complex, subunit B, iron sulfur (Ip) (SDHB), nuclear gene encoding mitochondrial protein, mRNA, NCBI [online], 2010 [retrieved on 2010-02-25]. Retrieved from the Internet:< URL: http://www.ncbi.nlm.nih.gov/nuccore/115387093>, pages 1-7). Attie et al. teach that their results can be used to design techniques for intervention in the progression of diabetes. One would be able to upregulate genes which would otherwise be in the process of downregulation and that this can be achieved by using gene therapy or by substances that induce genes (Attie et al., page 7, parag. 00027). Attie et al. teach that while the data was gathered in a mouse model, the data is largely useful in humans (Attie et al., page 8, parag. 00028).

With regard to the claims being drawn to practicing the method in skeletal muscle cells (claim 119), while Attie et al. teach that their study was carried out in adipose tissue (Attie et al., page 4, parag. 00014), they teach other tissues, such as muscle, liver, and pancreatic b-cells should also be studied to determine their role in diabetes (Attie et al., page 6, parag. 00021).

Applicant's arguments filed August 3, 2010 have been fully considered but they are not persuasive.

Applicant indicates that Attie et al. do not describe every element of the claimed invention. For example, Attie et al. do not describe contacting the cells with an agent and then determining whether expression of at least two OXPHOS-CR genes show a coordinate increase. Applicant indicates that Attie et al. teaches that it is possible to upregulate genes in mammals by adding additional copies of the gene to cells by gene therapy of by triggering upregulation of genes by introducing known substances into the individual (Attie page 7, parag. 27). Applicant indicates that these teachings do not describe contacting cells with an agent and then determining whether expression of at

least 2 OXPHOS-CR genes show a coordinate increase in cells. In response, this is not persuasive. Attie et al. meet the limitations of the claims as Attie et al. teach adding additional copies of genes to cells or using inducing substances that upregulate genes, wherein an invervention mechanism would prevent the progression into diabetic disease (Attie et al., page 7, parag. 0027). This meets the limitation of claim 93 a) with regard to contacting a test cell with an agent to be assessed for its ability to regulate gene expression. With regard to step b), an artisan would be "determining" whether or not gene expression constructs or inducing substances would in fact be increasing the expression levels of the downregualted diabetic genes of interest such that progression into diabetic disease is prevented.

Applicant indicates that Attie does not teach elements present in claims that depend on claim 93. For example, Attie does not teach that OXPHOS-CR genes are coordinately regulated and is silent regarding the existence, identification, or use of agents that cause a coordinate increase in the expression of at least two OXPHOS-CR gene products when contacted with a test cell. Attie does not and could not describe an agent that causes a coordinate increase in the expression of at least two OXPHOS-CR gene products, wherein the agent is a potential enhancer of Err-alpha or Gabp, or enhances mitochondrial biogenesis, and expression of Nuclear Respiratory Factor 1 (NRF-1)(Applicant's response, page 9). In response, this is not persuasive. The instant claims are drawn to screening and seeing whether or not compounds upregulate downregulated genes in diabetic patients (Attie et al., page 7, parag 0027). An artisan would recognize that these test compounds can be used singly, wherein one or more

downregulated diabetic genes are upregulated, or in combination, in order to arrive at an intervention mechanism that prevents the progression of diabetes. The claims do not require that the agent be an enhancer of Err-alpha or Gabp (claim 106) because the claims are drawn to determining whether or not any compound of interest can be used to treat diabetes and includes identifying compounds that do not upregulate downregulated diabetic genes. Claims 106-112, 115-121, 124-127 only indicate that the potential compound have a possible ability to have biological effects and using one (or more) gene(s) and/or a compound that upregulates downregulated diabetic genes taught by Attie et al. meet this limitation.

Applicant indicates that Attie's statement (parag. 0021) that changes in gene expression in adipose tissue might not be sufficient to cause diabetes and that alterations in muscle, liver, and pancreatic b-cells are probably also required does not teach that tissues should be studied as the Examiner contents. It merely comments that gene expression changes in such tissues are probably required to cause diabetes and does not describe determining whether skeletal muscle cells contacted with an agent exhibit a coordinate increase in expression of at least two OX-PHOS genes (Applicant's response, pages 9-10). In response, this is not persuasive. Attie et al.'s parag. 0027 teach that fat is not the only tissue affected in diabetes and that other tissues are affected in diabetes. Attie et al. teaching that muscle is affected is indicative that an artisan would look at other tissues, including muscle, in order to arrive at treatment of diabetes.

Thus, the claims remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 93, 118, 122-123 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Attie et al., WO 02/22886, published March 21, 2002, Scherf et al., 2000, Nature Genetics, 24: 236-244, for reasons of record, March 10, 2010.

For Applicant's convenience, the rejection of March 10, 2010 has been copied as follows.

As discussed above, Attie et al. teach that a microarray was used to determine the difference in expression of various genes in adipose tissue of obese and diabetic mouse models and those of wild type mice. Attie et al. teach that genes SDHB and CYC1 are downregulated in adipose tissue of mice. Attie et al. teach that their microarray results can be used to design techniques for the intervention in the progression of diabetes, wherein genes that are downregulated in the disease state can be upregulated.

While Attie et al. generally teach that downregulated genes can be upregulated, they do not specifically teach that designing techniques for the intervention of the progression of diabetes includes carrying out the method in parallel on multiple populations of cells and that each population is contacted with different agents (claims 122-123).

At the time of filing, the art teaches that gene expression levels in a number of cell lines can be measured simultaneously following their treatment with a library of compounds. For example, Scherf et al. teach that cDNA microarrays can be used to assess gene expression profiles of multiple cancer cell lines in a drug discovery screen (Scherf et al., abstract). Scherf et al. provides guidance that artisans were actively using microarrays to identify genes in various cell types that are affected in a disease state and are subsequently affected in the presence of a compound.

All of the component parts are taught in Attie et al. and Scherf et al. The only difference is the combination of the "old elements" into a single method of screening multiple populations of cells with different agents to be assessed.

It would have been obvious for an artisan to screen different chemical compounds on various cell types from diabetic patients in order to find chemical compounds that upregulate SDHB and CYC1. With regard to screening multiple tissue types, at the time of filing, Attie et al. teach that in addition to adipose tissue, an artisan can also look at other tissues that affect diabetes, such as muscle, liver, and pancreatic b-cells (Attie et al., page 6, parag. 00021). As such, an artisan would have included these tissue types with adipose tissue in order to identify any drug that would have a beneficial effect on treating diabetes. With regard to using a library of compounds (claim 123), Scherf et al. illustrate that large collections of candidate compounds are known in the art. It would have been obvious for an artisan to take large collections of compounds and test them on disease tissue in order to find compounds that ameliorate disease symptoms.

Applicant's arguments filed August 3, 2010 have been fully considered but they are not persuasive.

Applicant indicates that the Examiner asserts that Scherf provides guidance that artisans were actively using microarrays to identify genes in various cell types that are affected in a disease state and are subsequently affected in the presence of a compound. Applicant indicates that Scherf does not provide this guidance. First, Scherf used microarrays to obtain gene expression profiles from different cancer cell lines, and does not identify genes that are affected in cancer as compared with the non-diseased state. Scherf studied gene expression profiles in cell lines derived from a number of cancers (page 236, last sentence in left col.). Second, Scherf does not determine whether any of the genes that were affected in the presence of a compound are among the genes whose expression is affected in cancer (Applicant's response, pages 10-11). In response, this is not persuasive. While Applicant focuses on other issues taught by Scherf et al., the Examiner relied on Scherf et al. to teach that it is

routine to carry out a screening method in parallel on multiple populations of cells and that the cells can be contacted with different agents. Given Scherf et al.'s teaching an artisan would have adapted Scherf et al.'s teaching such that a number of other tissues affected by diabetes (e.g. muscle and liver taught by Attie et al.) can be screened simultaneously with a number of different compounds in order to find compounds that can be used to inhibit the progression of diabetes.

Applicant indicates that even if Attie and/or Scherf taught using microarrays to identify genes in various cell types and are affected in a disease state and are subsequently affected in the presence of a compound, it would not be obvious to screen different chemical compounds on various tissues from diabetic patients in order to upregulate SDHB and CYC1. Attie et al. teaches that many genes are shown here to be either upregulated or downregulated in adipose cells as an individual first becomes insulin resistant and then diabetic. Given that gene therapy is available to use this information to design intervention strategies, one would upregulate genes which would otherwise be in the process of downregulation (page 7, parag. 27). Attie does not describe intervening in the expression of any particular subset of the upregulated and/or downregulated genes. Even if Attie did, an artisan would recognize the difficulty of seeking an agent to simultaneously affect multiple independent upregulated and downregulated genes. Applicant indicates that Attie does not teach downregulation of SDHB and CYC1 in insulin resistance or diabetes. (Applicant's emphasis, Applicant's response, page 11). In response, this is not persuasive. Attie et al. teach that an artisan would take the list of upregulated and downregulated genes in diabetic patients

and upregulate the downregulated genes and downregulate the upregulated genes such that an artisan would arrive at a way of preventing progression of diabetes. With regard to Applicant indicating that there is difficulty in seeking an agent to simultaneously affect multiple independent upregulated and downregulated genes, this is not persuasive because an artisan would recognize that a compound that brings the expression of more genes to the level of normal patients would be more beneficial than a compound that brings fewer genes to the level of normal patients. With regard to Applicant indicating that Attie et al. does not teach downregulation of SDHB and CYC1 in particular stages of diabetes, the claims do not require that that the genes be downregulated at a particular stage of disease, or be downregulated for any specific disease.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Wednesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632